



R.E.D. FACTS

BROMOXYNIL

Pesticide Reregistration

All pesticides sold or distributed in the United States must be registered by EPA, based on scientific studies showing that they can be used without posing unreasonable risks to people or the environment. Because of advances in scientific knowledge, the law requires that pesticides which were first registered before November 1, 1984, be reregistered to ensure that they meet today's more stringent standards.

In evaluating pesticides for reregistration, EPA obtains and reviews a complete set of studies from pesticide producers, describing the human health and environmental effects of each pesticide. The Agency develops any mitigation measures or regulatory controls needed to effectively reduce each pesticide's risks. EPA then reregisters pesticides that can be used without posing unreasonable risks to human health or the environment.

When a pesticide is eligible for reregistration, EPA explains the basis for its decision in a Reregistration Eligibility Decision (RED) document. This fact sheet summarizes the information in the RED document for reregistration case 2070, bromoxynil.

Use Profile

Bromoxynil is a selective contact foliage applied herbicide used to control a variety of grasses and broadleaf weeds. Agricultural crop use sites include: food crops (e.g., garlic/onions); food and feed crops (e.g., mint, flax, spearmint, peppermint, barley, oats, rye, triticale, wheat, sorghum, cotton, and field, sweet, and pop corn); and feed crops (e.g., fodder/hay, grass, millet (proso), alfalfa, sudangrass). Non-food uses include: fallow/idleland; outdoor industrial areas; nonagricultural uncultivated areas/soils; ornamental herbaceous plants; commercial/industrial lawns; ornamental (non-residential) lawns and turf; golf course turf; and sod farms. Bromoxynil is formulated as an emulsifiable concentrate, soluble concentrate, and a gel formulation (in water soluble packages). The application rates for crop uses range from 0.25 lb ai/acre to 0.5 lb ai/acre. There are no residential uses for this herbicide.

Regulatory History

Bromoxynil was first registered in the United States in 1965 for use as a herbicide to control grassy and broadleaf weeds on wheat and barley. In 1972, tolerances were established for field and fodder crops, meat, and meat byproducts of cattle, goats, hogs, horses and sheep. Throughout the 1980's, a series of additional tolerances were established for a variety of vegetable, field and fodder crops.

When the reregistration case for bromoxynil was opened, case 2070, bromoxynil phenol, butyrate, heptanoate and octanoate were all incorporated. Subsequently, bromoxynil butyrate registrations were voluntarily canceled by the registrant in 1989 due to concerns related to developmental toxicity. Therefore, bromoxynil butyrate is not included as a part of this reregistration decision. At that time, the Agency also had concerns for potential risks to workers mixing, loading, and/or applying bromoxynil products. To reduce these exposures, the registrant undertook several actions. These included label amendments, development of a new jug (to prevent splashing) and the supply of gloves included in product packaging.

Further changes to the reregistration case came when the registrant decided not to support the heptanoate. However, in 1993, the registrant applied for a new heptanoate registration, which was granted. Since only those pesticides registered prior to 1984 are subject to reregistration, the bromoxynil heptanoate is not considered a reregistration chemical and is not specifically incorporated for this reregistration action. However, there are two products which include both the heptanoate and the octanoate forms of bromoxynil. All esters of the chemical are considered to be toxicologically similar to the phenol and, in fact, rapid conversion of the esters to the phenol occurs in the environment. The exposure estimates, therefore, incorporate exposure to the octanoate and the heptanoate included in the two combined labels. The percent crop treated used in the dietary exposure considers all esters of bromoxynil.

In May 1995 (60 FR 27414), the Agency established a time-limited tolerance under section 408 of the Federal Food, Drug and Cosmetic Act (FFDCA), for residues of bromoxynil on cottonseed. This tolerance expired on April 1, 1997. On May 13, 1998, the Agency issued a tolerance for cotton use. In that Notice, the maximum allowable cotton acreage that can be treated with bromoxynil was increased from 400,000 acres (3% of cotton acreage) to 1.3 million acres (10% of cotton acreage). This document incorporates the information published in the May 13, 1998 Federal Register Notice.

Human Health Toxicity Assessment

Bromoxynil phenol is in Toxicity Category II for acute effects via the oral and inhalation routes and Toxicity Category III for acute dermal effects. Bromoxynil octanoate is Toxicity Category II for acute oral and dermal effects and Toxicity Category III for acute inhalation effects. Bromoxynil phenol has been classified as a Group C, possible human carcinogen. Rapid conversion of the ester forms of the chemical (heptanoate and octanoate) permit the risk assessment to be based on exposure to the phenol. Bromoxynil is considered to be developmentally toxic. This concern is considered below under, FQPA Assessment.

Dietary Exposure and Risk

The Reference Dose (RfD) for bromoxynil phenol is 0.015 mg/kg/day based on the threshold NOEL/LOEL of 1.5 mg/kg/day in a 12 month-chronic oral toxicity study in dogs. Chronic non-cancer dietary risk is estimated to occupy less than one percent (1%) of the chronic RfD. The aggregate dietary risk of cancer to the general population from residues in food and water, associated with long-term exposure to bromoxynil, was estimated to be 1.7×10^{-6} . The estimated aggregate acute dietary risk, calculated as Margins of Exposure (MOE), all exceed 10,000. Therefore, significant concerns related to acute and chronic dietary exposure are not predicted.

Occupational and Residential Exposure and Risk

The handler dermal risk assessment based on the Pesticide Handler's Exposure Database (PHED) data for mixers/loaders/applicators indicates that short- and intermediate-term dermal risks and cancer risks are acceptable (i.e., greater than 100) if such handlers wear chemical-resistant gloves in addition to baseline attire (long-sleeve shirt, long pants, shoes, and socks) while performing mixing and loading tasks and baseline attire while performing applicator tasks. For all other tasks, the risks are acceptable for handlers wearing baseline attire. The cancer risk for the non-commercial handlers (grower) is 2×10^{-6} or lower for all scenarios with baseline attire, except that mixers and loaders must also wear chemical-resistant gloves. The cancer risk for commercial handlers is 1.9×10^{-5} or lower for all scenarios with baseline attire, except that mixers and loaders must also wear chemical-resistant gloves. The highest cancer risk estimate from these particular scenarios was 1.9×10^{-5} (commercial mixer/loaders for aerial applications and sprinkler irrigation). However, these mixer/loader risk estimates do not account for the potential exposure reduction from the use of "wide-mouth" containers (designed to reduce spillage) for mixer/loaders. At the present time the PHED database does not allow the Agency to quantify this risk mitigation measure, however the use of the "wide-mouth" containers would likely reduce the reported risk

further. In addition, to provide an additional margin of safety, EPA has required mixers and loaders to wear a chemical-resistant apron. Although EPA has no data to specifically assess the exposure reduction to mixers/loaders afforded by a chemical-resistant apron, the Agency is persuaded that the exposure reduction would be significant. Available data indicate that the preponderance of non-hand exposure to mixers/loaders is to the front torso.

FQPA Assessment

In accordance with the Food Quality Protection Act of 1996, the Agency uses a weight-of-evidence approach to determine whether to retain, reduce, or remove the 10X safety factor required for possible enhanced sensitivity to infants and children. The database for the developmental toxicity of bromoxynil is robust. Developmental effects (supernumerary ribs being the most sensitive indicator) have been observed in developmental and reproductive studies. The Agency concluded that reliable data support using a 100-fold uncertainty factor to assess bromoxynil dietary risk for all populations with the exception of females 13+. Upon review of the extensive developmental toxicological database for this chemical, a concern for *in utero* developmental effects was noted. In order to provide a sufficient margin of safety for the developing fetus, the 10-fold safety factor for enhanced sensitivity to infants and children was retained for females 13+ thus requiring a 1000-fold uncertainty factor for this population subgroup. All MOEs calculated exceeded 10,000 and, therefore, developmental effects to any sub-population are not predicted.

Environmental Assessment

Environmental Fate

Bromoxynil octanoate was found to be chemically and physically similar to bromoxynil heptanoate. Both esters rapidly degrade to bromoxynil *per se*. Bromoxynil octanoate is mobile and non-persistent. It dissipates in the environment by abiotic hydrolysis, photolytic degradation, and microbially-mediated metabolism in both the aerobic and anaerobic environments. Bromoxynil octanoate readily hydrolyzes to bromoxynil phenol and then further degrades to CO₂. The hydrolysis half-life for degradation of bromoxynil octanoate ranges from 1 day up to 34 days. Degradation is increased by exposure to sunlight and aerobic and anaerobic degradative processes.

Based on the available data, the Agency concludes that the potential for ground water contamination from bromoxynil octanoate is low; it does not exhibit the mobility or persistence characteristics of pesticides that are normally

found in ground water. Environmental fate studies indicate that bromoxynil (phenol and octanoate) should not persist in surface waters. The aerobic aquatic metabolism study shows rapid degradation with a half-life of <12 hours.

Ecological Effects

The overall risk to birds (and to insects) exposed to bromoxynil octanoate is expected to be low. For mammals the calculated risk ranges from medium to high, based on known developmental effects. However, exposure levels high enough to cause chronic developmental effects are believed to be unlikely to occur. The acute risk to both freshwater and estuarine fish is expected to be low; chronic risk is expected to be minimal. The overall acute risk to freshwater invertebrates is expected to be medium. The overall risk to both endangered and non-endangered terrestrial and semi-aquatic plants is expected to be medium. And finally, the risk to aquatic vascular plants is uncertain at this time due to a lack of data, while risk to nonvascular plants is expected to be minimal. Additional testing for aquatic vascular plants is required.

Risk Mitigation

As a result of this RED, the Agency does not have concerns relative to dietary exposure (including food and water), for the general population to bromoxynil. There are no residential uses of the chemical. However, based on calculations made for occupational uses, the Agency is requiring that chemical resistant gloves, in addition to baseline attire, be worn by handlers involved in mixing, loading and/or applying bromoxynil. In order to provide an additional margin of safety, mixers and loaders will also be required wear a chemical resistant apron. Finally, given the concern that the Agency identified for increased fetal susceptibility, the Agency is requiring that scouting activities be specifically included on labels for the restricted entry timeframes.

Additional Data Required

The Agency is requiring the submission of two confirmatory studies (aquatic plant toxicity and chronic estuarine/marine fish and invertebrates) to complete the database for bromoxynil. Also, in the case of one of the technicals, EPA is requiring that acute toxicity information be submitted. In addition, product-specific data including product chemistry and acute toxicity studies, product efficacy data, revised Confidential Statements of Formula (CSFs), and revised labeling for reregistration are being requested in this document. Additionally, in order to allow more precise estimates of exposure

to bromoxynil in drinking water, the Agency herein reiterates the requirement of the submission of an acceptable surface water monitoring program as specified in the FR Notice, 63FR26473.

Product Labeling Changes Required

(1) Plantback intervals. Pending receipt of limited field rotational crop studies for cotton, labels must restrict rotation of treated cotton fields, treated with more than 0.5 a.i./A/season, to transgenic cotton (BXN cotton).

(2) The following language must be placed on registered labels: "The restricted-entry interval (REI) for cotton is 4 days and includes scouts and crop advisors. The exemption in the Worker Protection Standard for certified crop advisors does not apply to bromoxynil. Scouts and crop advisors are prohibited from entering the treated area during the entire 4-day REI for bromoxynil. Applicators and other users must inform crop advisors and scouts of this requirement."

(3) EPA is establishing a 4-day REI for uses of bromoxynil on cotton and a 26-day REI for uses of bromoxynil on turf grown for transplanting (e.g., on sod farms). EPA believes that measures to reduce short- and intermediate-term risks also will reduce cancer risks. These REIs reconfirm the REIs of 4 days for cotton and 26 days for sod established in the Federal Register Notice published May 13, 1998, in conjunction with the cotton use registration action.

(4) EPA has required mixers and loaders to wear a chemical-resistant apron. Although EPA has no data to specifically assess the exposure reduction to mixers/loaders afforded by a chemical-resistant apron, the Agency is persuaded that the exposure reduction would be significant.

Regulatory Conclusion

Based on the reviews of the generic data for the active ingredient bromoxynil, the Agency has sufficient information on the health effects of bromoxynil and on its potential for causing adverse effects in fish and wildlife and the environment. The Agency has determined that bromoxynil products, labeled and used as specified in the Reregistration Eligibility Decision, will not pose unreasonable risks to humans or the environment. Therefore, the Agency concludes that products containing bromoxynil for all uses are eligible for reregistration, provided the registrant follows all requirements as set forth in the RED.

For More Information

EPA is requesting public comments on the Reregistration Eligibility Decision (RED) document for BROMOXYNIL during a 60-day time period,

as announced in a Notice of Availability published in the Federal Register. To obtain a copy of the RED document or to submit written comments, please contact the Pesticide Docket, Information and Record Integrity Branch, Information Resources Services Division (7502C), Office of Pesticide Programs (OPP), US EPA, Washington, DC 20460, telephone 703-305-5805.

Electronic copies of the RED and this fact sheet are available on the internet. See <http://www.epa.gov/REDS>.

Printed copies of the RED and fact sheet can be obtained from EPA's National Center for Environmental Publications and Information (EPA/NCEPI), PO Box 42419, Cincinnati, OH 45242-0419, telephone 513-489-8190, fax 513-489-8695.

Following the comment period, the BROMOXYNIL RED document also will be available from the National Technical Information Service (NTIS), 5285 Port Royal Road, Springfield, VA 22161, telephone 703-605-6000 or 800-553-6847.

For more information about EPA's pesticide reregistration program, the BROMOXYNIL RED, or reregistration of individual products containing bromoxynil, please contact the Special Review and Reregistration Division (7508W), OPP, US EPA, Washington, DC 20460, telephone 703-308-8000.

For information about the health effects of pesticides, or for assistance in recognizing and managing pesticide poisoning symptoms, please contact the National Pesticides Telecommunications Network (NPTN). Call toll-free 1-800-858-7378, between 9:30 am and 7:30 pm Eastern Standard Time, Monday through Friday.